

What is claimed is:

1. An isolated mutant IgE protein, wherein mutant IgE_{HC} proteins of said mutant IgE protein have reduced spatial mobility compared to the spatial mobility of unmodified IgE_{HC} proteins in an unmodified IgE protein, wherein said unmodified IgE_{HC}'s comprise the amino acid sequence of SEQ ID NO:11.
2. The isolated mutant IgE protein of Claim 1, wherein said mutant IgE protein is constrained to the open conformation or the closed conformation.
3. The isolated mutant IgE protein of Claim 1, wherein the N-terminal amino-acids residues of the Ce3 domains of said mutant IgE_{HC} proteins are unable to obtain an inter-residue distance of 23Å or more.
4. The isolated mutant IgE protein of Claim 1, wherein the N-terminal amino-acids residues of the Ce3 domains of said mutant IgE_{HC} proteins have a fixed, inter-residue distance of between about 13 Å and less than 23 Å.
5. The isolated mutant IgE protein of Claim 1, wherein said mutant IgE protein is constrained in a conformation in which the N-terminal amino-acids residues of the Ce3 domains of said IgE_{HC} proteins have an inter-residue distance selected from the group consisting of a distance of about 13Å, a distance of about 14Å, a distance of about 15Å, a distance of about 16Å, a distance of about 17Å, a distance of about 18Å, a distance of about 19Å, a distance of about 20Å, a distance of about 21Å a distance of about 22Å or a distance of between about 22 Å and less than 23Å.
6. The isolated mutant IgE protein of Claim 1, wherein said mutant IgE protein comprises a IgE_{HC} protein that comprises an amino acid sequence at least about 80% identical to SEQ ID NO:11, wherein the amino acid in said protein corresponding to position 2, 3, 4, 5, 6, 7, 8 or 9 or SEQ ID NO:11 is a cysteine or methionine.
7. The isolated mutant IgE protein of Claim 6, wherein said mutant IgE protein binds to an antibody raised against an IgE protein comprising an unmodified IgE_{HC} comprising the amino acid sequence of SEQ ID NO:11.
8. The isolated mutant IgE protein of Claim 1, wherein said mutant IgE_{HC} proteins comprise an amino acid sequence selected from the group consisting of SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25 and SEQ ID NO:27.
9. An isolated nucleic acid molecule comprising a nucleic acid sequence at least about 80% identical to SEQ ID NO:10, wherein the codon in said nucleic acid

sequence corresponding to nucleotides 4-6, 7-9, 10-12, 13-15, 16-18, 19-21, 22-24, or 25-27 of SEQ ID NO:10 encodes a cysteine or a methionine.

10. The isolated nucleic acid molecule of Claim 9, wherein said nucleic acid molecule comprises a nucleic acid sequence selected from the group consisting of:

5 (a) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 4-6 of said nucleic acid sequence encodes a cysteine or a methionine;

10 (b) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 7-9 of said nucleic acid sequence encodes a cysteine or a methionine;

15 (c) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 10-12 of said nucleic acid sequence encodes a cysteine or a methionine;

20 (d) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 13-15 of said nucleic acid sequence encodes a cysteine or a methionine;

(e) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 16-18 of said nucleic acid sequence encodes a cysteine or a methionine;

25 (f) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 19-21 of said nucleic acid sequence encodes a cysteine or a methionine;

(g) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 22-24 of said nucleic acid sequence encodes a cysteine or a methionine; and

20 (h) a nucleic acid sequence at least about 90% identical to SEQ ID NO:10, wherein the codon at nucleotides 25-27 of said nucleic acid sequence encodes a cysteine or a methionine.

11. The isolated nucleic acid molecule of Claim 9, wherein said nucleic acid 30 sequence encodes a protein having an amino acid sequence at least about 80% identical to SEQ ID NO:11, wherein the amino acid in said protein corresponding to position 2, 3, 4, 5, 6, 7, 8 or 9 or SEQ ID NO:11 is a cysteine or methionine and wherein said protein

binds an antibody raised against a protein having the amino acid sequence of SEQ ID NO:11.

12. The isolated nucleic acid molecule of Claim 9, wherein said nucleic acid sequence is selected from the group consisting of SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24 and SEQ ID NO:26.

13. An isolated protein having an amino acid sequence at least about 80% identical to SEQ ID NO:11, wherein the amino acid in said protein corresponding to position 2, 3, 4, 5, 6, 7, 8 or 9 of SEQ ID NO:11 is a cysteine or methionine and wherein 10 said protein binds to an antibody raised against a protein having the amino acid sequence of SEQ ID NO:11.

14. The isolated protein of Claim 13, wherein said protein comprises an amino acid sequence selected from the group consisting of:

(a) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 2 of such amino acid sequence is a cysteine or a methionine;

(b) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 3 of such amino acid sequence is a cysteine or a methionine;

20 (c) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 4 of such amino acid sequence is a cysteine or a methionine;

(d) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 5 of such amino acid sequence is a cysteine or 25 a methionine;

(e) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 6 of such amino acid sequence is a cysteine or a methionine;

30 (f) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 7 of such amino acid sequence is a cysteine or a methionine;

(g) an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid at position 8 of such amino acid sequence is a cysteine or a methionine; and

(h) an amino acid sequence at least about 90% identical to SEQ ID 5 NO:11, wherein the amino acid at position 9 of such amino acid sequence is a cysteine or a methionine.

15. The isolated protein of Claim 13, wherein said protein comprises an amino acid sequence selected from SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25 and SEQ ID NO:17.

10 16. A method selected from the group consisting of:

(a) a method to identify a compound that inhibits the binding of IgE to a Fc ϵ RI, said method comprising:

(i) contacting an isolated mutant IgE protein of Claim 1 or an isolated protein of Claim 13 with a putative inhibitory compound in the presence of a 15 Fc ϵ RI or Fc ϵ RI α protein; and

(ii) determining if said putative inhibitory compound inhibits the binding of said mutant IgE protein of Claim 1 or said isolated protein of Claim 13 to said Fc ϵ RI or Fc ϵ RI α protein; and

(b) a method to identify a compound that binds to IgE either in or 20 resulting in a closed conformation, said method comprising:

(i) contacting an isolated mutant IgE protein of Claim 1 or an isolated protein of Claim 13 with a putative inhibitory compound in the presence of a Fc ϵ RI or Fc ϵ RI α protein; and

(ii) determining if said putative inhibitory compound binds to 25 said mutant IgE protein of Claim 1 or said isolated protein of Claim 13.

17. The method of Claim 16, wherein said mutated IgE molecule comprises IgE_{HC}'s comprising an amino acid sequence at least about 90% identical to SEQ ID NO:11, wherein the amino acid in said protein corresponding to position 2,3 ,4, 5, 6, 7, 8 or 9 or SEQ ID NO:11 is a cysteine or methionine and wherein said protein binds an 30 antibody raised against a protein having the amino acid sequence of SEQ ID NO:11.

18. An isolated compound that inhibits the binding of IgE to an Fc ϵ RI, wherein said compound is identified by the method of Claim 16.

19. The isolated compound of Claim 18, wherein said compound does not bind the open form of IgE.
20. A composition comprising the compound of Claim 18 and an excipient.
21. A method to protect an animal from a disease mediated by IgE, said
5 method comprising administering a composition of Claim 20.
22. A kit comprising an isolated mutant IgE protein of Claim 1 or an isolated protein of Claim 13 and a means to determine if a compound binds to said isolated mutant IgE protein of Claim 1 or said isolated protein of Claim 13.